

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-8, 11, 15, 16, 26, 40-42, 49, 70-75, and 82-85 are pending in the application, with claim 1 being the sole independent claim. Claim 1 is amended to recite the step of differentiating embryonic stem cells into cardiomyocytes and further co-culturing with fibroblasts. Support for the amendments can be found throughout the specification, *inter alia*, in Example 2. Claim 45 is sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 82-85 are sought to be added. Support for the new claims can be found throughout the specification, *inter alia*, in the claims as originally filed. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Double Patenting***

The provisional rejection of claims 1-5, 40-42, and 49 on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 3-7 of co-pending US Application No. 11/547,871 was maintained. Applicants respectfully request that the rejection be held in abeyance until subject matter that is otherwise allowable is identified, at which time Applicants will consider filing a terminal disclaimer to obviate the rejection.

The provisional rejection of claims 1, 6, 8, 11, 15, 16, 26, 45, and 49 on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 3, 17, 21-24, 26-32, 47, 55, 57-62, 64-69, and 70 of copending US Application No. 10/594,188 was maintained. Applicants respectfully request that the rejection be held in abeyance until subject matter that is otherwise allowable is identified, at which time Applicants will consider filing a terminal disclaimer to obviate the rejection.

***Rejections under 35 U.S.C. § 102***

The rejection of claims 1, 2, 4, 5, 7, 8, 11, 15, 16, 26, 40, 41, 45, 49, and 70-73, under 35 U.S.C. § 102(b) as allegedly anticipated by Muller (Muller *et al.* FASEB J 14:2540-2548), as evidenced by Itskovitz-Eldor (Itskovitz-Eldor *et al.* Molecular Medicine 6(2):88-95, 2000) was maintained. Applicants respectfully traverse the rejection especially as it may be applied to the amended claims presented herein.

The Examiner maintains that Muller's disclosure of embryoid body (EB) differentiation culture inherently includes the production of fibroblasts in addition to endothelial cells and cardiomyocytes. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution Applicants have amended claim 1 to incorporate the initial step of differentiating embryonic stem (ES) cells into cardiomyocytes. Applicants have also amended the claim to be directed to co-culturing the cardiomyocytes with fibroblasts to promote contractile cardiac tissue. Applicants respectfully assert that since Muller does not expressly or inherently disclose a culture system in which ES cells differentiate into cardiomyocytes, and further into contractile

cardiac tissue, Muller does not anticipate the claims presented herein. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

The rejection of claims 1, 2, 3-5, 7, 8, 11, 15, 16, 26, 40, 41, 45, 49, and 70-74 under 35 U.S.C. § 102(b) as allegedly being anticipated by Franz (U.S. Patent No. 5,928,943) was maintained. Applicants respectfully traverse the rejection especially as it may be applied to the amended claims presented herein.

The Examiner maintains that Franz's disclosure of an EB culture system with ES cells discloses each of the claimed limitations. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution Applicants have amended claim 1 to incorporate the initial step of differentiating embryonic stem (ES) cells into cardiomyocytes and co-culturing the cardiomyocytes with fibroblasts to promote contractile cardiac tissue. Applicants respectfully assert that since Franz does not expressly or inherently disclose a culture system in which ES cells differentiate into cardiomyocytes, and further co-culturing to produce contractile cardiac tissue, Franz does not anticipate the claims presented herein. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

### ***Rejections under 35 U.S.C. § 103***

The rejection of claims 1, 3, 6, 42, and 75 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Franz (cited above), in further view of Wantanabe (Wantanabe *et al.* Biochem Biophys Res Com 213(1):130-137, 1995), Muller (cited above) and Feld (Feld *et al.* Circulation 105:522-529, January 2002) was maintained. Applicants

respectfully traverse the rejection especially as it may be applied to the amended claims presented herein.

Applicants respectfully assert that an ordinary artisan reading Franz, in view of Wantanabe, Muller, and Feld would not have predictably arrived at the presently claimed method of obtaining cardiac tissue. As amended, claim 1 is directed to a method of modeling or obtaining cardiac tissue comprising (a) differentiating embryonic stem (ES) cells into cardiomyocytes; (b) co-culturing the cardiomyocytes obtained in step (a) with fibroblasts; and (c) allowing integration and alignment of the cardiomyocytes and fibroblasts into cardiac tissue; wherein the cardiomyocytes acquire longitudinal morphology upon integration and alignment with the fibroblasts; and wherein said cardiac tissue exhibits contractility.

In contrast, Franz is directed to the generation of EB using ES cells and not a method of obtaining cardiac tissue by culturing cardiomyocytes and fibroblasts. Muller is directed towards a method of culturing mouse embryonic stem cells to form cardiomyocytes. Muller does not disclose a method of obtaining contractile cardiac tissue by culturing cardiomyocytes with fibroblasts. Thus, one of ordinary skill in the art would not have looked to either Franz or Muller for guidance to develop a predictable method to obtain cardiac tissue that exhibits contractility. Watanabe and Feld, either individually or in combination, do not cure the deficiencies of Franz. As discussed previously, neither Wantanabe nor Feld suggest culturing cardiomyocytes in the presence of fibroblasts to form cardiac tissue. Therefore, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness and respectfully request that this rejection be reconsidered and withdrawn.

***Rejections under 35 U.S.C. § 112, second paragraph***

Claims 1-8, 11, 15, 16, 26, 40-42, 45, 49, and 70-75, as amended or previously presented, are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Examiner alleges that the term "a tissue-like structure" is unclear. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended claim 1 to remove the term. Therefore, the rejection has been rendered moot and Applicants respectfully request that the rejection be reconsidered and withdrawn.

***Claim objections***

Claims 1, 15, and 72 are objected to because of informalities. The claims have been amended as suggested by the Examiner. Accordingly, Applicants respectfully request that the objections be withdrawn.

***Rejections under 35 U.S.C. § 112, first paragraph***

Claims 1-8, 11, 15, 16, 26, 40-42, 45, 49, and 70-75 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges that the description of the cardiac tissue as exhibiting "cross-striation" constitutes new matter. Example 2 demonstrates co-cultivation of ES cell-derived cardiac cells and fibroblasts to produce cardiac tissue. However, not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended the claims to delete the reference to culture of cardiomyocytes, endothelial cells, and fibroblasts which results in cross- Atty. Dkt. No. 2590.0030002/EJH/PAC

striated cardiac tissue. Therefore, Applicants respectfully assert that the claims as amended as adequately described and respectfully request that the rejection be reconsidered and withdrawn.

Claims 1-8, 11, 15, 16, 26, 40-42, 45, 49, and 70-75 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. The Examiner alleges that while the specification is enabled for obtaining cardiac tissue by a method comprising culturing cardiomyocytes, it is not enabled for a method that uses differentiating cardiomyocytes, differentiating fibroblasts, and differentiating endothelial cells. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended the claims to delete the reference of using differentiating cardiomyocytes, differentiating fibroblasts, and differentiating endothelial cells in the method. Therefore, Applicants respectfully assert that the claims are enabled and respectfully request that the rejection be reconsidered and withdrawn.

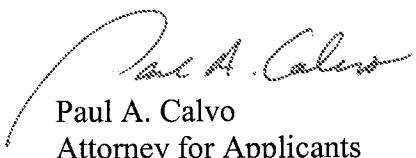
***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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